Appl. No.

: 09/787,356

**Filed** 

June 25, 2001

## AMENDMENTS TO THE CLAIMS

- 1. (Currently amended) A method for mediating relaxation of an airway of an animal, said method comprising administering to said animal, an effective amount an amount of a peptide effective for mediating relaxation of said airway, of a said peptide having a sequence comprising SLIGRL (SEQ ID NO:2) or a peptide analog thereof in which an amino acid is replaced with a non-natural amino acid, wherein said peptide is capable of activating an airway epithelium protease activated receptor-2 (PAR2) under conditions sufficient for activation of said PAR2 to occur, thereby mediating relaxation of said airway.
  - 2. (Cancelled)
  - 3. (Cancelled)
  - 4. (Cancelled)
- 5. (Currently amended) The method according to Claim 1 wherein the inflammation relaxation of the airway is caused by a disease condition selected from the group consisting of asthma, bronchitis, hayfever, alveolitis, ciliary dyskinesis and pulmonary inflammation.
- 6. (Previously presented)The method according to Claim 1 wherein the peptide comprises the sequence of SEQ ID NO.2.
- 7. (Previously presented)The method according to Claim 6 wherein the peptide is modified to permit entry across an epithelial and/or subcutaneous layer.
- 8. (Previously presented)The method according to Claim 7 wherein the peptide is fused to penetratin.
- 9. (Previously presented)The method according to Claim 7 wherein the peptide is fused to TAT.

Claims 10-19 (Cancelled)

20. (Currently amended) A method of identifying an agent for treatment or prophylaxis of inflammation of an airway of an animal, comprising:

exposing PAR2 to the agent; and

measuring the ability of the agent to activate the PAR2, wherein the agent is identified as capable of being useful for said treatment or prophylaxis of inflammation of an airway of an animal if it does have the ability to activate PAR2; and

Appl. No. Filed

09/787,356

: June 25, 2001

further testing the peptide for treatment or prophylaxis of inflammation of an airway of an animal if it is identified as being useful.

(Previously presented) The method of Claim 1, wherein said peptide incorporates a 21. non-natural amino acid.

(Previously presented) The method of Claim 1, wherein said peptide incorporates a 22. non-natural amino acid listed in the following table:

| Non-conventional amino acid               | Code  | Non-conventional amino acid | Code  |
|---|-------|-----------------------------|-------|
| α-aminobutyric acid                       | Abu   | L-N-methylalanine           | Nmala |
| $\alpha$ -amino- $\alpha$ -methylbutyrate | Mgabu | L-N-methylarginine          | Nmarg |
| aminocyclopropane-                        | Cpro  | L-N-methylasparagine        | Nmasn |
| carboxylate                               |       | L-N-methylaspartic acid     | Nmasp |
| aminoisobutyric acid                      | Aib   | L-N-methylcysteine          | Nmcys |
| aminonorbornyl-                           | Norb  | L-N-methylglutamine         | Nmgln |
| carboxylate                               |       | L-N-methylglutamic acid     | Nmglu |
| cyclohexylalanine                         | Chexa | L-N-methylhistidine         | Nmhis |
| cyclopentylalanine                        | Cpen  | L-N-methylisoleucine        | Nmile |
| D-alanine                                 | Dal   | L-N-methylleucine           | Nmleu |
| D-arginine                                | Darg  | L-N-methyllysine            | Nmlys |
| D-aspartic acid                           | Dasp  | L-N-methylmethionine        | Nmmet |
| D-cysteine                                | Dcys  | L-N-methylnorleucine        | Nmnle |
| D-glutamine                               | Dgln  | L-N-methyinorvaline         | Nmnva |
| D-glutamic acid                           | Dglu  | L-N-methylornithine         | Nmorn |
| D-histidine                               | Dhis  | L-N-methylphenylalanine     | Nmphe |
| D-isoleucine                              | Dile  | L-N-methylproline           | Nmpro |
| D-leucine                                 | Dleu  | L-N-methylserine            | Nmser |
| D-lysine                                  | Dlys  | L-N-methylthreonine         | Nmthr |
| D-methionine                              | Dmet  | L-N-methyltryptophan        | Nmtrp |
| D-ornithine                               | Dorn  | L-N-methyltyrosine          | Nmtyr |
| D-phenylalanine                           | Dphe  | L-N-methylvaline            | Nmval |
| D-proline                                 | Dpro  | L-N-methylethylglycine      | Nmetg |

Appl. No.

: 09/787,356

Filed

June 25, 2001

Non-conventional amino acid Code Non-conventional amino acid Code Dser L-N-methyl-t-butylglycine Nmtbug D-serine Nle L-norleucine D-threonine Dthr D-tryptophan L-norvaline Nva Dtrp α-methyl-aminoisobutyrate Maib D-tyrosine Dtyr Mgabu D-valine Dval  $\alpha$ -methyl- $\gamma$ -aminobutyrate Mchexa Dmala α-methylcyclohexylalanine D-α-methylalanine Mcpen D-α-methylarginine Dmarg α-methylcylcopentylalanine Manap D-α-methylasparagine Dmasn  $\alpha$ -methyl- $\alpha$ -napthylalanine α-methylpenicillamine Mpen  $D-\alpha$ -methylaspartate Dmasp N-(4-aminobutyl)glycine Nglu D-α-methylcysteine Dmcys Naeg N-(2-aminoethyl)glycine D-α-methylglutamine Dmgln N-(3-aminopropyl)glycine Norn **Dmhis**  $D-\alpha$ -methylhistidine Nmaabu Dmile N-amino-α-methylbutyrate D-α-methylisoleucine Dmleu α-napthylalanine Anap D-α-methylleucine N-benzylglycine Nphe D-α-methyllysine Dmlys N-(2-carbamylethyl)glycine Ngln  $D-\alpha$ -methylmethionine Dmmet Dmorn N-(carbamylmethyl)glycine Nasn  $D-\alpha$ -methylornithine Dmphe N-(2-carboxyethyl)glycine Nglu D-α-methylphenylaianine N-(carboxymethyl)glycine D-α-methylproline Dmpro Nasp Ncbut N-cyclobutylglycine D-α-methylserine Dmser Dmthr N-cycloheptylglycine Nchep D-α-methylthreonine N-cyclohexylglycine Nchex D-α-methyltryptophan **Dmtrp** Ncdec Dmty N-cyclodecylglycine  $D-\alpha$ -methyltyrosine N-cylcododecylglycine Ncdod D-α-methylvaline Dmval N-cyclooctylglycine Ncoct D-N-methylalanine Dnmala Ncpro D-N-methylarginine Dnmarg N-cyclopropylglycine Ncund N-cycloundecylglycine D-N-methylasparagine Dnmasn N-(2,2-diphenylethyl)glycine Nbhm D-N-methylaspartate Dnmasp

Appl. No. Filed 09/787,356 June 25, 2001

| D-N-methylglutamine Dnmgln N-(3-guanidinopropyl)glycine Narg D-N-methylglutamate Dnmglu N-(1-hydroxyethyl)glycine Nthr D-N-methylhistidine Dnmhis N-(hydroxyethyl)glycine Nser D-N-methyllisoleucine Dnmile N-(imidazolylethyl)glycine Nhis D-N-methylleucine Dnmleu N-(3-indolylyethyl)glycine Nhtrp D-N-methyllysine Dnmlys N-methyl-γ-aminobutyrate Nmgabu N-methylcyclohexylalanine Nmchexa D-N-methylmethionine Dnmmet D-N-methylgroine Nala D-N-methylphenylaianine Dnmphe N-methylglycine Nala D-N-methylproline Dnmpro N-(1-methylpropyl)glycine Nile D-N-methyltreonine Dnmser N-(2-methylpropyl)glycine Nleu D-N-methyltreonine Dnmthr D-N-methyltryosine Dnmtrp N-(1-methylethyl)glycine Nval D-N-methyltryosine Dnmtry N-methyla-napthylaianine Nmanap D-N-methylvaline Dnmval N-methylpenicillamine Nmpen γ-aminobutyric acid Gabu N-(ρ-hydroxyphenyl)glycine Ntyr L-t-butylglycine Etg penicillamine Pen L-α-methylarginine Marg L-α-methylasparagine Masn L-α-methylasparate Masp L-α-methylglycine Metg L-α-methylglutamine Mgln L-α-methylglycine Metg L-α-methylglutamine Mgln L-α-methylglycine Nmpet L-α-methylisoleucine Mile N-(2-methylthioethyl)glycine Nmpet Mlys  | Non-conventional amino acid | Code    | Non-conventional amino acid   | Code   |
|---|-----------------------------|---------|-------------------------------|--------|
| D-N-methylglutamate Dnmglu N-(1-hydroxyethyl)glycine Nthr D-N-methylhistidine Dnmhis N-(hydroxyethyl)glycine Nser D-N-methylisoleucine Dnmile N-(imidazolylethyl)glycine Nhis D-N-methylleucine DnmIeu N-(3-indolylycthyl)glycine Nhtrp D-N-methyllysine Dnmlys N-methyl-γ-aminobutyrate Nmgabu N-methylcyclohexylalanine Dnmorn N-methylcyclopentylalanine Dnmorn N-methylgycine Nala D-N-methylphenylaianine Dnmphe N-methylgycine Nala D-N-methylphenylaianine Dnmphe N-methylaminoisobutyrate Nmaib D-N-methylproline Dnmpro N-(1-methylpropyl)glycine Nile D-N-methylserine Dnmser N-(2-methylpropyl)glycine Nleu D-N-methylthreonine Dnmthr D-N-methyltryptophan Dnmtrp N-(1-methylethyl)glycine Nval D-N-methyltyrosine Dnmtyr N-methyla-napthylaianine Nmanap D-N-methylvaline Dnmval N-methylpenicillamine Nmpen γ-aminobutyric acid Gabu N-(ρ-hydroxyphenyl)glycine Ntyr L-t-butylglycine Tbug N-(thiomethyl)glycine Ncys L-ethylglycine Etg penicillamine Mala L-α-methylarginine Marg L-α-methylasparate Masp L-α-methylasparate Masp L-α-methylglycine Metg L-α-methylglycine Metg L-α-methylglycine Mibu N-(2-methylthioethyl)glycine Nmet L-α-methylglucine Mile N-(2-methylthioethyl)glycine Nmet Mhphe | D-N-methylcysteine          | Dnmcys  | N-(3,3-diphenylpropyl)glycine | Nbhe   |
| D-N-methylhistidine D-N-methylhistidine D-N-methylisoleucine D-N-methylisoleucine D-N-methyllisoleucine N-methyloriithine D-N-methylisoleucine N-methylgycine N-methylgycine N-methylgycine N-methylaminoisobutyrate N-maib D-N-methylproline D-N-methylpropyl)glycine N-(1-methylpropyl)glycine N-(2-methylpropyl)glycine N-(2-methyltryptophan D-N-methyltryptophan D-N-methyltrysoine D-N-methyltyrosine D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylproicillamine N-(p-hydroxyphenyl)glycine N-(t-i-butylglycine L-t-butylglycine L-t-butylglycine L-t-methylarginine L-α-methylarginine Marg L-α-methylarginine Marg L-α-methylaspartate Masp L-α-methyletylglycine Metg L-α-methylglutamine Mgln L-α-methylglutamine Mglu L-α-methyllistidine Mhis L-α-methyllisoleucine Mile N-(2-methyllysine Mlys  | D-N-methylglutamine         | Dnmgln  | N-(3-guanidinopropyl)glycine  | Narg   |
| D-N-methylisoleucine Dnmile N-(imidazolylethyl))glycine Nhis D-N-methylleucine Dnmleu N-(3-indolylyethyl)glycine Nhtrp D-N-methyllysine Dnmlys N-methyl-γ-aminobutyrate Nmgabu N-methylcyclohexylalanine Nmchexa D-N-methylmethionine Dnmmet D-N-methylgrine Nala D-N-methylpenylalanine Nmcpen N-methylgycine Nala D-N-methylproline Dnmpro N-methylgropyl)glycine Nile D-N-methylproline Dnmpro N-(1-methylpropyl)glycine Nile D-N-methyltreonine Dnmthr N-(2-methylpropyl)glycine Nleu D-N-methyltreonine Dnmthr D-N-methyltrystophan Dnmtrp N-(1-methylethyl)glycine Nval D-N-methyltrystopine Dnmtyr N-methyla-napthylaianine Nmanap D-N-methyltryiosine Dnmval N-methylpenicillamine Nmpen γ-aminobutyric acid Gabu N-(ρ-hydroxyphenyl)glycine Ncys L-t-butylglycine Etg penicillamine Pen L-homophenylalanine Hphe L-α-methylanine Mash L-α-methylaspartate Masp L-α-methyletylglycine Metg L-α-methylglycine Mglu L-α-methylglycine Mglu L-α-methylglycine Mglu L-α-methylglycine Mglu L-α-methyllisidine Mhis L-α-methyllsioleucine Mile N-(2-methyllsine Mlys   | D-N-methylglutamate         | Dnmglu  | N-(1 -hydroxyethyl)glycine    | Nthr   |
| D-N-methylleucine Dnmleu N-(3-indolylyethyl)glycine Nhttp D-N-methyllysine Dnmlys N-methyl-γ-aminobutyrate Nmgabu N-methylcyclohexylalanine Dnmorn N-methylcyclopentylalanine Nmcpen N-methylglycine Nala D-N-methylphenylaianine Dnmphe N-methylaminoisobutyrate Nmaib D-N-methylproline Dnmpro N-(1-methylpropyl)glycine Nile D-N-methylserine Dnmser N-(2-methylpropyl)glycine Nleu D-N-methylthreonine Dnmthr D-N-methyltryptophan Dnmtrp N-(1-methylethyl)glycine Nval D-N-methyltyrosine Dnmtyr N-methyla-napthylaianine Nmanap D-N-methylvaline Dnmval N-methylpenicillamine Nmpen γ-aminobutyric acid Gabu N-(ρ-hydroxyphenyl)glycine Ntyr L-t-butylglycine Tbug N-(thiomethyl)glycine Ncys L-ethylglycine Etg penicillamine Pen L-homophenylalanine Hphe L-α-methylasparagine Masn L-α-methylaspartate Masp L-α-methyl-t-butylglycine Metg L-α-methylgyteine Mgln L-α-methylglutamate Mglu L-α-methylglutamine Mgln L-α-methyllophycine Nmet L-α-methylisidine Mhis L-α-methyllysine Nmet L-α-methylisidine Mile N-(2-methylthioethyl)glycine Nmet L-α-methyllsoleucine Mile N-(2-methyllysine Milys   | D-N-methylhistidine         | Dnmhis  | N-(hydroxyethyl))glycine      | Nser   |
| D-N-methyllysine Dnmlys N-methyl-γ-aminobutyrate Nmgabu N-methylcyclohexylalanine Nmchexa D-N-methylmethionine Dnmmet D-N-methylgycine Nala D-N-methylphenylaianine Dnmphe N-methylgycine Nala D-N-methylphenylaianine Dnmphe N-methylgycine Nile D-N-methylproline Dnmpro N-(1 -methylpropyl)glycine Nile D-N-methylserine Dnmser N-(2-methylpropyl)glycine Nleu D-N-methyltreonine Dnmthr D-N-methyltryptophan Dnmtrp N-(1 -methylethyl)glycine Nval D-N-methyltryptophan Dnmtyr N-methyla-napthylaianine Nmanap D-N-methylvaline Dnmval N-methylpenicillamine Nmpen γ-aminobutyric acid Gabu N-(ρ-hydroxyphenyl)glycine Nttyr L-t-butylglycine Etg penicillamine Ncys L-ethylglycine Etg penicillamine Pen L-homophenylalanine Marg L-α-methylalanine Mala L-α-methylasparate Masp L-α-methyl-t-butylglycine Mtbug L-α-methylcysteine Mcys L-methylglycine Metg L-α-methylglycine Mgln L-α-methylglycine Mglu L-α-methyllistidine Mhis L-α-methylhomophenylaianine Mphe L-α-methyllistoleucine Mile N-(2-methyllysine Nmet L-α-methyllistoleucine Mile N-(2-methyllysine Milys Mlys  | D-N-methylisoleucine        | Dnmile  | N-(imidazolylethyl))glycine   | Nhis   |
| N-methylcyclohexylalanineNmchexaD-N-methylmethionineDnmmetD-N-methylornithineDnmornN-methylcyclopentylalanineNmcpenN-methylglycineNalaD-N-methylphenylaianineDnmpheN-methylaminoisobutyrateNmaibD-N-methylprolineDnmproN-(1 -methylpropyl)glycineNileD-N-methylserineDnmserN-(2-methylpropyl)glycineNleuD-N-methyltreonineDnmthrD-N-methyltryptophanDnmtrpN-(1 -methylethyl)glycineNvalD-N-methyltyrosineDnmtyrN-methyla-napthylaianineNmanapD-N-methylvalineDnmvalN-methylpenicillamineNmpenγ-aminobutyric acidGabuN-(ρ-hydroxyphenyl)glycineNhtyrL-t-butylglycineEtgpenicillamineNcysL-ethylglycineEtgpenicillaminePenL-homophenylalanineHpheL-α-methylasparagineMasnL-α-methylarginineMargL-α-methylasparagineMasnL-α-methylcysteineMcysL-methylethylglycineMtbugL-α-methylcysteineMcysL-methylethylglycineMetgL-α-methylglutamineMgluL-α-methylglutamateMgluL-α-methylhistidineMhisL-α-methylhioethyl)glycineNmetL-α-methyllsoleucineMileN-(2-methylthioethyl)glycineNmetL-α-methylleucineMleuL-α-methyllysineMllys   | D-N-methylleucine           | Dnmleu  | N-(3-indolylyethyl)glycine    | Nhtrp  |
| D-N-methylornithine Dnmorn N-methylcyclopentylalanine Nmcpen N-methylglycine Nala D-N-methylphenylaianine Dnmphe N-methylgminoisobutyrate Nmaib D-N-methylproline Dnmpro N-(1-methylpropyl)glycine Nile D-N-methylserine Dnmser N-(2-methylpropyl)glycine Nleu D-N-methylthreonine Dnmthr D-N-methyltryptophan Dnmtrp N-(1-methylethyl)glycine Nval D-N-methyltyrosine Dnmtyr N-methyla-napthylaianine Nmanap D-N-methylvaline Dnmval N-methylpenicillamine Nmpen γ-aminobutyric acid Gabu N-(ρ-hydroxyphenyl)glycine Ncys L-ethylglycine Etg penicillamine Pen L-homophenylalanine Hphe L-α-methylalanine Mala L-α-methylarginine Marg L-α-methylasparagine Masn L-α-methylcysteine Mcys L-methylglycine Metg L-α-methylglycine Metg L-α-methylglutamine Mgln L-α-methylglutamate Mglu L-α-methylistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methylisoleucine Mile N-(2-methyllysine Nmet Mlys   | D-N-methyllysine            | Dnmlys  | N-methyl-γ-aminobutyrate      | Nmgabu |
| N-methylglycineNalaD-N-methylphenylaianineDnmpheN-methylaminoisobutyrateNmaibD-N-methylprolineDnmproN-(1 -methylpropyl)glycineNileD-N-methylserineDnmserN-(2-methylpropyl)glycineNleuD-N-methylthreonineDnmthrD-N-methyltryptophanDnmtrpN-(1 -methylethyl)glycineNvalD-N-methyltyrosineDnmtyrN-methyla-napthylaianineNmanapD-N-methylvalineDnmvalN-methylpenicillamineNmpenγ-aminobutyric acidGabuN-(ρ-hydroxyphenyl)glycineNhtyrL-t-butylglycineTbugN-(thiomethyl)glycineNcysL-ethylglycineEtgpenicillaminePenL-homophenylalanineHpheL-α-methylalanineMalaL-α-methylarginineMargL-α-methylalanineMasnL-α-methylaspartateMaspL-α-methyl-t-butylglycineMtbugL-α-methylcysteineMcysL-methylethylglycineMetgL-α-methylglutamineMglnL-α-methylglutamateMgluL-α-methyllistidineMhisL-α-methylhomophenylaianineMhpheL-α-methylisoleucineMileN-(2-methyllhoethyl)glycineNmetL-α-methylleucineMleuL-α-methyllysineNmet  | N-methylcyclohexylalanine   | Nmchexa | D-N-methylmethionine          | Dnmmet |
| N-methylaminoisobutyrateNmaibD-N-methylprolineDnmproN-(1 -methylpropyl)glycineNileD-N-methylserineDnmserN-(2-methylpropyl)glycineNleuD-N-methylthreonineDnmthrD-N-methyltryptophanDnmtrpN-(1 -methylethyl)glycineNvalD-N-methyltyrosineDnmtyrN-methyla-napthylaianineNmanapD-N-methylvalineDnmvalN-methylpenicillamineNmpenγ-aminobutyric acidGabuN-(ρ-hydroxyphenyl)glycineNhtyrL-t-butylglycineTbugN-(thiomethyl)glycineNcysL-ethylglycineEtgpenicillaminePenL-homophenylalanineHpheL-α-methylalanineMalaL-α-methylarginineMargL-α-methylasparagineMasnL-α-methylaspartateMaspL-α-methyl-t-butylglycineMtbugL-α-methylcysteineMcysL-methylethylglycineMetgL-α-methylglutamineMglnL-α-methylglutamateMgluL-α-methylhistidineMhisL-α-methylhomophenylaianineMhpheL-α-methyllisoleucineMileN-(2-methylthioethyl)glycineNmetL-α-methylleucineMleuL-α-methyllysineMlys   | D-N-methylornithine         | Dnmorn  | N-methylcyclopentylalanine    | Nmcpen |
| N-(1 -methylpropyl)glycineNileD-N-methylserineDnmserN-(2-methylpropyl)glycineNleuD-N-methylthreonineDnmthrD-N-methyltryptophanDnmtrpN-(1 -methylethyl)glycineNvalD-N-methyltyrosineDnmtyrN-methyla-napthylaianineNmanapD-N-methylvalineDnmvalN-methylpenicillamineNmpenγ-aminobutyric acidGabuN-(ρ-hydroxyphenyl)glycineNhtyrL-t-butylglycineTbugN-(thiomethyl)glycineNcysL-ethylglycineEtgpenicillaminePenL-homophenylalanineHpheL-α-methylalanineMalaL-α-methylarginineMargL-α-methylasparagineMasnL-α-methylaspartateMaspL-α-methylethylglycineMtbugL-α-methylgutamineMglnL-α-methylglycineMetgL-α-methyllistidineMhisL-α-methyllydutamateMgluL-α-methylistoleucineMileN-(2-methyllhioethyl)glycineNmetL-α-methylleucineMileN-(2-methyllysineMlys  | N-methylglycine             | Nala    | D-N-methylphenylaianine       | Dnmphe |
| N-(2-methylpropyl)glycineNleuD-N-methylthreonineDnmthrD-N-methyltryptophanDnmtrpN-(1-methylethyl)glycineNvalD-N-methyltyrosineDnmtyrN-methyla-napthylaianineNmanapD-N-methylvalineDnmvalN-methylpenicillamineNmpenY-aminobutyric acidGabuN-(p-hydroxyphenyl)glycineNhtyrL-t-butylglycineTbugN-(thiomethyl)glycineNcysL-ethylglycineEtgpenicillaminePenL-homophenylalanineHpheL-α-methylalanineMalaL-α-methylarginineMargL-α-methylasparagineMasnL-α-methylaspartateMaspL-α-methyl-t-butylglycineMtbugL-α-methylglycineMetgL-α-methylglutamineMglnL-α-methylglycineMetgL-α-methylhistidineMhisL-α-methylhomophenylaianineMhpheL-α-methylisoleucineMileN-(2-methylthioethyl)glycineNmetL-α-methylleucineMleuL-α-methyllysineMlys  | N-methylaminoisobutyrate    | Nmaib   | D-N-methylproline             | Dnmpro |
| D-N-methyltryptophan D-N-methyltyrosine D-N-methyltyrosine D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylvaline D-N-methylpenicillamine Nmpen N-(p-hydroxyphenyl)glycine Nhtyr L-t-butylglycine D-N-methylpenicillamine N-(p-hydroxyphenyl)glycine Ncys L-ethylglycine D-N-methylglycine D-N-methylglycine N-(p-hydroxyphenyl)glycine Ncys L-ethylglycine Ncys L-ethylglycine D-N-methylglycine N-cys N-(thiomethyl)glycine Ncys L-ethylglycine N-c-methylalanine Mala L-α-methylarginine Marg L-α-methylasparagine Masn L-α-methylaspartate Masp L-α-methyl-t-butylglycine Metg L-α-methylglycine Metg L-α-methylglycine Metg L-α-methylglutamine Mglu L-α-methylhistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methyllsoleucine Mile N-(2-methyllysine Milys  | N-(1 -methylpropyl)glycine  | Nile    | D-N-methylserine              | Dnmser |
| D-N-methyltyrosine Dnmtyr N-methyla-napthylaianine Nmanap D-N-methylvaline Dnmval N-methylpenicillamine Nmpen γ-aminobutyric acid Gabu N-(ρ-hydroxyphenyl)glycine Nhtyr L-t-butylglycine Tbug N-(thiomethyl)glycine Ncys L-ethylglycine Etg penicillamine Pen L-homophenylalanine Hphe L-α-methylalanine Mala L-α-methylarginine Marg L-α-methylasparagine Masn L-α-methylaspartate Masp L-α-methyl-t-butylglycine Mtbug L-α-methylcysteine Mcys L-methylglycine Metg L-α-methylglutamine Mgln L-α-methylglutamate Mglu L-α-methylhistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methylisoleucine Mile N-(2-methyllysine Mlys Mlys  | N-(2-methylpropyl)glycine   | Nleu    | D-N-methylthreonine           | Dnmthr |
| D-N-methylvaline  P-aminobutyric acid  Gabu  N-(ρ-hydroxyphenyl)glycine  Nhtyr  L-t-butylglycine  Tbug  N-(thiomethyl)glycine  Neys  L-ethylglycine  Etg  penicillamine  Pen  L-homophenylalanine  Hphe  L-α-methylalanine  Marg  L-α-methylasparagine  Masn  L-α-methylaspartate  Masp  L-α-methyl-t-butylglycine  Metg  L-α-methylcysteine  Metg  L-α-methylglutamine  Mgln  L-α-methylglutamate  Mglu  L-α-methylhistidine  Mile  N-(2-methyllysine  Mlys  Mlys  | D-N-methyltryptophan        | Dnmtrp  | N-(1 -methylethyl)glycine     | Nval   |
| γ-aminobutyric acidGabuN-(ρ-hydroxyphenyl)glycineNhtyrL-t-butylglycineTbugN-(thiomethyl)glycineNcysL-ethylglycineEtgpenicillaminePenL-homophenylalanineHpheL-α-methylalanineMalaL-α-methylarginineMargL-α-methylasparagineMasnL-α-methylaspartateMaspL-α-methyl-t-butylglycineMtbugL-α-methylcysteineMcysL-methylethylglycineMetgL-α-methylglutamineMglnL-α-methylglutamateMgluL-α-methylhistidineMhisL-α-methylhomophenylaianineMhpheL-α-methylisoleucineMileN-(2-methylthioethyl)glycineNmetL-α-methylleucineMleuL-α-methyllysineMlys   | D-N-methyltyrosine          | Dnmtyr  | N-methyla-napthylaianine      | Nmanap |
| L-t-butylglycine  L-ethylglycine  Etg  penicillamine  Pen  L-homophenylalanine  Hphe  L-α-methylalanine  Masn  L-α-methylaspartate  L-α-methylaspartate  Masp  L-α-methyl-t-butylglycine  Metg  L-α-methylglycine  Metg  L-α-methylglutamine  Mgln  L-α-methylglutamate  Mglu  L-α-methylistidine  Mile  N-(2-methyllysine  Mlys  Mlys  | D-N-methylvaline            | Dnmval  | N-methylpenicillamine         | Nmpen  |
| L-ethylglycineEtgpenicillaminePenL-homophenylalanineHpheL-α-methylalanineMalaL-α-methylarginineMargL-α-methylasparagineMasnL-α-methylaspartateMaspL-α-methyl-t-butylglycineMtbugL-α-methylcysteineMcysL-methylethylglycineMetgL-α-methylglutamineMglnL-α-methylglutamateMgluL-α-methylhistidineMhisL-α-methylhomophenylaianineMhpheL-α-methylisoleucineMileN-(2-methylthioethyl)glycineNmetL-α-methylleucineMleuL-α-methyllysineMlys  | γ-aminobutyric acid         | Gabu    | N-(ρ-hydroxyphenyl)glycine    | Nhtyr  |
| L-homophenylalanine Hphe L-α-methylalanine Mala L-α-methylarginine Marg L-α-methylasparagine Masn L-α-methylaspartate Masp L-α-methyl-t-butylglycine Mtbug L-α-methylcysteine Mcys L-methylethylglycine Metg L-α-methylglutamine Mgln L-α-methylglutamate Mglu L-α-methylhistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methylisoleucine Mile N-(2-methylthioethyl)glycine Nmet L-α-methylleucine Mleu L-α-methyllysine Mlys  | L-t-butylglycine            | Tbug    | N-(thiomethyl)glycine         | Ncys   |
| L-α-methylarginine Marg L-α-methylasparagine Masn L-α-methylaspartate Masp L-α-methyl-t-butylglycine Mtbug L-α-methylcysteine Mcys L-methylethylglycine Metg L-α-methylglutamine Mgln L-α-methylglutamate Mglu L-α-methylhistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methylisoleucine Mile N-(2-methylhioethyl)glycine Nmet L-α-methylleucine Mleu L-α-methyllysine Mlys   | L-ethylglycine              | Etg     | penicillamine                 | Pen    |
| L-α-methylaspartate  Masp  L-α-methyl-t-butylglycine  Metg  L-α-methylglutamine  Mgln  L-α-methylglutamate  Mglu  L-α-methylhistidine  Mhis  L-α-methylhomophenylaianine  Mhphe  L-α-methylisoleucine  Mile  N-(2-methylhioethyl)glycine  Mlys  | L-homophenylalanine         | Hphe    | L-α-methylalanine             | Mala   |
| L-α-methylcysteine Mcys L-methylethylglycine Metg L-α-methylglutamine Mgln L-α-methylglutamate Mglu L-α-methylhistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methylisoleucine Mile N-(2-methylthioethyl)glycine Nmet L-α-methylleucine Mleu L-α-methyllysine Mlys   | L-α-methylarginine          | Marg    | L-α-methylasparagine          | Masn   |
| L-α-methylglutamine Mgln L-α-methylglutamate Mglu L-α-methylhistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methylisoleucine Mile N-(2-methylthioethyl)glycine Nmet L-α-methylleucine Mleu L-α-methyllysine Mlys   | L-α-methylaspartate         | Masp    | L-α-methyl-t-butylglycine     | Mtbug  |
| L-α-methylhistidine Mhis L-α-methylhomophenylaianine Mhphe L-α-methylisoleucine Mile N-(2-methylthioethyl)glycine Nmet L-α-methylleucine Mleu L-α-methyllysine Mlys   | L-α-methylcysteine          | Mcys    | L-methylethylglycine          | Metg   |
| L-α-methylisoleucine Mile N-(2-methylthioethyl)glycine Nmet L-α-methylleucine Mleu L-α-methyllysine Mlys  | L-α-methylglutamine         | Mgln    | L-α-methylglutamate           | Mglu   |
| L-α-methylleucine Mleu L-α-methyllysine Mlys  | L-α-methylhistidine         | Mhis    | L-α-methylhomophenylaianine   | Mhphe  |
|   | L-α-methylisoleucine        | Mile    | N-(2-methylthioethyl)glycine  | Nmet   |
| L-α-methylmethionine Mmet L-α-methylnorleucine Mnle   | L-α-methylleucine           | Mleu    | L-α-methyllysine              | Mlys   |
|   | L-α-methylmethionine        | Mmet    | L-α-methylnorleucine          | Mnle   |

Appl. No.

: 09/787,356

Filed

June 25, 2001

| Non-conventional amino acid  | Code  | Non-conventional amino acid | Code   |
|------------------------------|-------|-----------------------------|--------|
| L-α-methyinorvaline          | Mnva  | L-α-methylornithine         | Morn   |
| L-α-methylphenylalanine      | Mphe  | L-α-methylproline           | Mpro   |
| L-a-methylserine             | Mser  | L-α-methylthreonine         | Mthr   |
| L-α-methyltryptophan         | Mtrp  | L-a-methyltyrosine          | Mtyr   |
| L-α-methylvaline             | Mval  | L-N-methylhomophenylaianine | Nmhphe |
| N-(N-(2,2-diphenylethyl)     | Nnbhm | N-(N-(3,3-diphenylpropyl)   | Nnbhe  |
| carbamyimethyl)glycine       |       | carbamylmethyl)glycine      |        |
| 1 -carboxy-1 -(2,2-diphenyl- | Nmbc  |                             |        |
| ethylamino)cyclopropane      |       |                             |        |

## 23. (Cancelled)

24. (Currently amended) A method for prophylaxis or treatment of inflammation of an airway of an animal, said method comprising administering to said animal, an effective amount for said an amount of a peptide effective for prophylaxis or treatment of a inflammation, said peptide having a sequence comprising SLIGRL (SEQ ID NO:2) or a peptide analog thereof in which an amino acid is replaced with a non-natural amino acid, wherein said peptide is capable of activating an airway epithelium protease activated receptor-2 (PAR2) under conditions sufficient for activation of said PAR2 to occur, thereby providing said prophylaxis or treatment of inflammation.

## 25. (Cancelled)

- 26. (Previously presented)The method according to Claim 24 wherein the inflammation of the airway is caused by a disease condition selected from the group consisting of asthma, bronchitis, hayfever, alveolitis, ciliary dyskinesis and pulmonary inflammation.
- 27. (Previously presented)The method according to Claim 24 wherein the peptide comprises the sequence of SEQ ID NO.2.
- 28. (Previously presented)The method according to Claim 27 wherein the peptide is modified to permit entry across an epithelial and/or subcutaneous layer.
- 29. (Previously presented)The method according to Claim 27 wherein the peptide is fused to penetratin.

Appl. No. : 09/787,356 Filed : June 25, 2001

- 30. (Previously presented)The method according to Claim 27 wherein the peptide is fused to TAT.
  - 31. (Cancelled)
- 32. (Previously presented)The method of Claim 24, wherein said peptide incorporates a non-natural amino acid listed in the following table:

| Non-conventional amino acid               | Code  | Non-conventional amino acid | Code   |
|---|-------|-----------------------------|--------|
| α-aminobutyric acid                       | Abu   | L-N-methylalanine           | Nmala  |
| $\alpha$ -amino- $\alpha$ -methylbutyrate | Mgabu | L-N-methylarginine          | Nmarg  |
| aminocyclopropane-                        | Cpro  | L-N-methylasparagine        | Nmasn  |
| carboxylate                               |       | L-N-methylaspartic acid     | Nmasp  |
| aminoisobutyric acid                      | Aib   | L-N-methylcysteine          | Nmcys  |
| aminonorbornyl-                           | Norb  | L-N-methylglutamine         | Nmgln  |
| carboxylate                               |       | L-N-methylglutamic acid     | Nmglu  |
| cyclohexylalanine                         | Chexa | L-N-methylhistidine         | Nmhis  |
| cyclopentylalanine                        | Cpen  | L-N-methylisoleucine        | Nmile  |
| D-alanine                                 | Dal   | L-N-methylleucine           | Nmleu  |
| D-arginine                                | Darg  | L-N-methyllysine            | Nmlys  |
| D-aspartic acid                           | Dasp  | L-N-methylmethionine        | Nmmet  |
| D-cysteine                                | Deys  | L-N-methylnorleucine        | Nmnle  |
| D-glutamine                               | Dgln  | L-N-methyinorvaline         | Nmnva  |
| D-glutamic acid                           | Dglu  | L-N-methylornithine         | Nmorn  |
| D-histidine                               | Dhis  | L-N-methylphenylalanine     | Nmphe  |
| D-isoleucine                              | Dile  | L-N-methylproline           | Nmpro  |
| D-leucine                                 | Dleu  | L-N-methylserine            | Nmser  |
| D-lysine                                  | Dlys  | L-N-methylthreonine         | Nmthr  |
| D-methionine                              | Dmet  | L-N-methyltryptophan        | Nmtrp  |
| D-ornithine                               | Dorn  | L-N-methyltyrosine          | Nmtyr  |
| D-phenylalanine                           | Dphe  | L-N-methylvaline            | Nmval  |
| D-proline                                 | Dpro  | L-N-methylethylglycine      | Nmetg  |
| D-serine                                  | Dser  | L-N-methyl-t-butylglycine   | Nmtbug |
|   |       |                             |        |

Appl. No. Filed

: 09/7

•

09/787,356 June 25, 2001

| Non-conventional amino acid | Code   | Non-conventional amino acid                | Code   |
|-----------------------------|--------|--|--------|
| D-threonine                 | Dthr   | L-norleucine                               | Nle    |
| D-tryptophan                | Dtrp   | L-norvaline                                | Nva    |
| D-tyrosine                  | Dtyr   | $\alpha$ -methyl-aminoisobutyrate          | Maib   |
| D-valine                    | Dval   | α-methyl-γ-aminobutyrate                   | Mgabu  |
| D-α-methylalanine           | Dmala  | $\alpha$ -methylcyclohexylalanine          | Mchexa |
| D-α-methylarginine          | Dmarg  | α-methylcylcopentylalanine                 | Mcpen  |
| D-α-methylasparagine        | Dmasn  | $\alpha$ -methyl- $\alpha$ -napthylalanine | Manap  |
| D-α-methylaspartate         | Dmasp  | α-methylpenicillamine                      | Mpen   |
| D-α-methylcysteine          | Dmcys  | N-(4-aminobutyl)glycine                    | Nglu   |
| D-α-methylglutamine         | Dmgln  | N-(2-aminoethyl)glycine                    | Naeg   |
| D-α-methylhistidine         | Dmhis  | N-(3-aminopropyl)glycine                   | Norn   |
| D-α-methylisoleucine        | Dmile  | N-amino-α-methylbutyrate                   | Nmaabu |
| D-α-methylleucine           | Dmleu  | α-napthylalanine                           | Anap   |
| D-α-methyllysine            | Dmlys  | N-benzylglycine                            | Nphe   |
| D-α-methylmethionine        | Dmmet  | N-(2-carbamylethyl)glycine                 | Ngln   |
| D-α-methylornithine         | Dmorn  | N-(carbamylmethyl)glycine                  | Nasn   |
| D-α-methylphenylaianine     | Dmphe  | N-(2-carboxyethyl)glycine                  | Nglu   |
| D-α-methylproline           | Dmpro  | N-(carboxymethyl)glycine                   | Nasp   |
| D-α-methylserine            | Dmser  | N-cyclobutylglycine                        | Ncbut  |
| D-α-methylthreonine         | Dmthr  | N-cycloheptylglycine                       | Nchep  |
| D-α-methyltryptophan        | Dmtrp  | N-cyclohexylglycine                        | Nchex  |
| D-α-methyltyrosine          | Dmty   | N-cyclodecylglycine                        | Ncdec  |
| D-α-methylvaline            | Dmval  | N-cylcododecylglycine                      | Ncdod  |
| D-N-methylalanine           | Dnmala | N-cyclooctylglycine                        | Ncoct  |
| D-N-methylarginine          | Dnmarg | N-cyclopropylglycine                       | Ncpro  |
| D-N-methylasparagine        | Dnmasn | N-cycloundecylglycine                      | Neund  |
| D-N-methylaspartate         | Dnmasp | N-(2,2-diphenylethyl)glycine               | Nbhm   |
| D-N-methylcysteine          | Dnmcys | N-(3,3-diphenylpropyl)glycine              | Nbhe   |

Appl. No. Filed 09/787,356 June 25, 2001

| Non-conventional amino acid | Code    | Non-conventional amino acid  | Code   |
|-----------------------------|---------|------------------------------|--------|
| D-N-methylglutamine         | Dnmgln  | N-(3-guanidinopropyl)glycine | Narg   |
| D-N-methylglutamate         | Dnmglu  | N-(1 -hydroxyethyl)glycine   | Nthr   |
| D-N-methylhistidine         | Dnmhis  | N-(hydroxyethyl))glycine     | Nser   |
| D-N-methylisoleucine        | Dnmile  | N-(imidazolylethyl))glycine  | Nhis   |
| D-N-methylleucine           | Dnmleu  | N-(3-indolylyethyl)glycine   | Nhtrp  |
| D-N-methyllysine            | Dnmlys  | N-methyl-γ-aminobutyrate     | Nmgabu |
| N-methylcyclohexylalanine   | Nmchexa | D-N-methylmethionine         | Dnmmet |
| D-N-methylornithine         | Dnmorn  | N-methylcyclopentylalanine   | Nmcpen |
| N-methylglycine             | Nala    | D-N-methylphenylaianine      | Dnmphe |
| N-methylaminoisobutyrate    | Nmaib   | D-N-methylproline            | Dnmpro |
| N-(1 -methylpropyl)glycine  | Nile    | D-N-methylserine             | Dnmser |
| N-(2-methylpropyl)glycine   | Nleu    | D-N-methylthreonine          | Dnmthr |
| D-N-methyltryptophan        | Dnmtrp  | N-(1 -methylethyl)glycine    | Nval   |
| D-N-methyltyrosine          | Dnmtyr  | N-methyla-napthylaianine     | Nmanap |
| D-N-methylvaline            | Dnmval  | N-methylpenicillamine        | Nmpen  |
| γ-aminobutyric acid         | Gabu    | N-(ρ-hydroxyphenyl)glycine   | Nhtyr  |
| L-t-butylglycine            | Tbug    | N-(thiomethyl)glycine        | Ncys   |
| L-ethylglycine              | Etg     | penicillamine                | Pen    |
| L-homophenylalanine         | Hphe    | L-α-methylalanine            | Mala   |
| L-α-methylarginine          | Marg    | L-α-methylasparagine         | Masn   |
| L-α-methylaspartate         | Masp    | L-α-methyl-t-butylglycine    | Mtbug  |
| L-α-methylcysteine          | Mcys    | L-methylethylglycine         | Metg   |
| L-α-methylglutamine         | Mgln    | L-α-methylglutamate          | Mglu   |
| L-α-methylhistidine         | Mhis    | L-α-methylhomophenylaianine  | Mhphe  |
| L-α-methylisoleucine        | Mile    | N-(2-methylthioethyl)glycine | Nmet   |
| L-α-methylleucine           | Mleu    | L-α-methyllysine             | Mlys   |
| L-α-methylmethionine        | Mmet    | L-α-methylnorleucine         | Mnle   |
| L-α-methyinorvaline         | Mnva    | L-α-methylornithine          | Morn   |
|                             |         |                              |        |

Appl. No. Filed

09/787,356 June 25, 2001

| Non-conventional amino acid  | Code  | Non-conventional amino acid | Code   |
|------------------------------|-------|-----------------------------|--------|
| L-α-methylphenylalanine      | Mphe  | L-α-methylproline           | Mpro   |
| L-a-methylserine             | Mser  | L-α-methylthreonine         | Mthr   |
| L-α-methyltryptophan         | Mtrp  | L-a-methyltyrosine          | Mtyr   |
| L-α-methylvaline             | Mval  | L-N-methylhomophenylaianine | Nmhphe |
| N-(N-(2,2-diphenylethyl)     | Nnbhm | N-(N-(3,3-diphenylpropyl)   | Nnbhe  |
| carbamyimethyl)glycine       |       | carbamylmethyl)glycine      |        |
| 1 -carboxy-1 -(2,2-diphenyl- | Nmbc  |                             |        |
| ethylamino)cyclopropane      |       |                             |        |